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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,762	WALHOUT ET AL.	
	Examiner	Art Unit	
	MICHELE K. JOIKE	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-17 are pending and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the strain, YM4271, is required to practice the invention. As such, the strain must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the strain. In the instant case, the process to generate the strain that is disclosed in the specification does not appear to be repeatable, nor does it appear the strain is readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would

satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;

c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;

d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

e) the deposit will be replaced if it should ever become inviable.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 11, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walhout et al in view of Fields et al and in further view of Sugawara et al.

Walhout et al (Methods in Enz. 328: 575-592, 2000, specifically pp.578-582 and Figure 2, Table 1) teach Gateway® cloning to study protein interaction. A vector is made with att sites flanking the ORF, for example, the *ccdB* gene. The att sites allow for integration into the genome of the cell. There can be two vectors for protein interaction mapping, pDB and pAD. Each can contain an antibiotic resistance marker, such as gentamycin or ampicillin. These vectors are transformed into a yeast cell. Table 1 lists the genes, which are at least 250 bp long, and includes some that are more than 500 bp long. However, they do not teach assessing activation of the reporter protein, a HIS3 or lacZ reporter gene or the YM4271 strain.

Fields et al (Nature 340: 245-246, 1989, see entire paper) teach a yeast two hybrid assay using a DBD and a TAD. The reporters are HIS3 and lacZ. They teach that when the proteins interact, transcription of the lacZ gene occurs, and the transcriptional activation can be measured by β-galactosidase activity. Transformants can also be grown on media lacking histidine. However, they do not teach the YM4271 strain.

Sugawara et al (Med. Sci. Monit. 8(11):BR431-8, 2002, specifically BR431 abd BR432) teach use of YM4271 in a screening method based on a yeast one-hybrid using HIS3 as a marker.

The ordinary skilled artisan, desiring to identify a protein that binds to a bait element that is flanked by att sites, would have been motivated to combine the teachings of Walhout et al teaching Gateway® cloning to study protein interaction with a vector made with att sites flanking the ORF with the teachings of Fields et al teaching a yeast two-hybrid and Sugawara et al teaching the use of YM4271 because Walhout et al state that this system allows for large numbers of ORFs to be conveniently cloned into different vectors, which is extremely useful. Additionally, Fields et al teach that identifying protein interactions could be of value in designing therapeutic peptides. Also, Sugawara et al teach that YM4271 is a HIS3 auxotroph, which is desirable for using a HIS3 marker. It would have been obvious to one of ordinary skill in the art to use a method to identify a protein that binds to a bait element is flanked by att sites because Walhout et al teach that the system allows for transfer of ORFs into different vectors or integration into the genome which makes it amenable to automation, which is

crucial for large-scale ORFeome cloning. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walhout et al, Fields et al and Sugawara et al as applied to claims 1-7, 11, 12 and 13 above, and further in view of Luo et al.

Walhout et al, Fields et al and Sugawara et al teach all of the limitations as described above. However, they do not teach using a mammalian cell.

Luo et al (Biotechniques 22(2): 350-352, 1997, specifically p. 350) teach a mammalian two-hybrid.

The ordinary skilled artisan, desiring to identify a protein that binds to a bait element that is flanked by att sites in a mammalian cell, would have been motivated to combine the teachings of Walhout et al teaching Gateway® cloning to study protein interaction with a vector made with att sites flanking the ORF with the teachings of Fields et al teaching a yeast two-hybrid, Sugawara et al teaching the use of YM4271 and Luo et al teaching a mammalian two-hybrid, because Luo et al state that protein interactions in mammalian cells may better mimic actual in vivo interactions. It would have been obvious to one of ordinary skill in the art to use mammalian cells because Luo et al teach that results can be obtained within 48 hours of transfection. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the

applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walhout et al, Fields et al and Sugawara et al as applied to claims 1-7, 11, 12 and 13 above, and further in view of Chalfie et al.

Walhout et al, Fields et al and Sugawara et al teach all of the limitations as described above. However, they do not teach using GFP.

Chalfie et al (Science 263: 802-805, 1994, specifically p. 803) teach GFP as a marker for gene expression.

The ordinary skilled artisan, desiring to use GFP, would have been motivated to combine the teachings of Walhout et al teaching Gateway® cloning to study protein interaction with a vector made with att sites flanking the ORF with the teachings of Fields et al teaching a yeast two-hybrid, Sugawara et al teaching the use of YM4271 and Chalfie et al teaching GFP as a marker for gene expression, because Chalfie et al state that detection of intracellular GFP requires only irradiation and is not limited by the availability of substrates. It would have been obvious to one of ordinary skill in the art to use GFP because Chalfie et al teach that GFP does not appear to interfere with cell growth and function. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent

evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walhout et al, Fields et al and Sugawara et al as applied to claims 1-7, 11, 12 and 13 above, and further in view of Cost et al.

Walhout et al, Fields et al and Sugawara et al teach all of the limitations as described above. However, they do not teach using assessing activation by determining the color of yeast cells.

Cost et al (Yeast 12: 939-941, 1996, specifically p. 939) teach using MET15 as a marker in yeast. Methionine auxotrophs produce a dark color in the presence of Pb^{2+}.

The ordinary skilled artisan, desiring to use MET15, would have been motivated to combine the teachings of Walhout et al teaching Gateway® cloning to study protein interaction with a vector made with att sites flanking the ORF with the teachings of Fields et al teaching a yeast two-hybrid, Sugawara et al teaching the use of YM4271 and Cost et al teaching using MET15 as a marker in yeast, because Cost et al state that the combination of the size of MET15, along with its counter-selectability and the color of *met15* mutations make this perhaps the most versatile yeast genetic marker. It would have been obvious to one of ordinary skill in the art to use MET15 because Cost et al teach that MET15 is useful for genetic screens. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be

considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walhout et al, Fields et al and Sugawara et al as applied to claims 1-7, 11, 12 and 13 above, and further in view of US 5,965,368.

Walhout et al, Fields et al and Sugawara et al teach all of the limitations as described above. However, they do not teach selecting a cell in which the reporter is activated and isolating the cDNA encoding the activation domain, and then sequencing the cDNA.

US 5,965,368 (specifically summary of invention and columns 35 and 36) teach a reverse two-hybrid wherein a cell, in which the reporter is activated, is selected, and the cDNA encoding the activation domain is isolated, and then sequenced. Mutant activation domains (Ads) were sequenced.

The ordinary skilled artisan, desiring to select a cell in which the reporter is activated and isolate the cDNA encoding the activation domain, and then sequence the cDNA, would have been motivated to combine the teachings of Walhout et al teaching Gateway® cloning to study protein interaction with a vector made with att sites flanking the ORF with the teachings of Fields et al teaching a yeast two-hybrid, Sugawara et al teaching the use of YM4271 and US 5,965,368 teaching a reverse two-hybrid wherein a cell, in which the reporter is activated, is selected, and the cDNA encoding the activation domain is isolated, and then sequenced, because US 5,965,368 state that there is value

in verifying if there is a correlation between the mutations in the AD and the phenotype of the cell. It would have been obvious to one of ordinary skill in the art to isolate and sequence the cDNA because sequencing the AD can determine the type of mutation, if one is present. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Walhout et al, Fields et al and Sugawara et al as applied to claims 1-7, 11, 12 and 13 above, and further in view of US 5,525,490.

Walhout et al, Fields et al and Sugawara et al teach all of the limitations as described above. However, they do not teach evaluating the effect of a test compound.

US 5,525,490 (specifically Abstract and columns 3-7) teach a reverse two hybrid to screen for molecules that inhibit a protein-protein interaction.

The ordinary skilled artisan, desiring to evaluate the effect of a test compound, would have been motivated to combine the teachings of Walhout et al teaching Gateway® cloning to study protein interaction with a vector made with att sites flanking the ORF with the teachings of Fields et al teaching a yeast two-hybrid and Sugawara et al teaching the use of YM4271, with the teachings of US 5,525,490 teaching a reverse two hybrid to screen for molecules that inhibit the protein-protein interaction, because US 5,525,490 states that there is a need for compositions and methods which can be

used to efficiently identify agents that specifically alter the intermolecular association between two polypeptides. It would have been obvious to one of ordinary skill in the art to screen for molecules that inhibit the protein-protein interaction because US 5,525,490 teach that there is a need to identify inhibitors with satisfactory sensitivity. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K Joike, Ph.D./

Michele K Joike, Ph.D.
Examiner
Art Unit 1636